

CLAIMS

1. An anhydrous form of sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide (Anhydrous Form B)
5 having an X-ray powder diffraction pattern containing specific peaks at: 3.8 ($\pm 0.1^\circ$), 7.5 ($\pm 0.1^\circ$), 11.2 ($\pm 0.1^\circ$), 13.0 ($\pm 0.1^\circ$), 13.8 ($\pm 0.1^\circ$), 15.0 ($\pm 0.1^\circ$), 15.7 ($\pm 0.1^\circ$), 18.8 ($\pm 0.1^\circ$), 20.2 ($\pm 0.1^\circ$), 21.7 ($\pm 0.1^\circ$), 22.6 ($\pm 0.1^\circ$) and 30.2 ($\pm 0.1^\circ$) 2θ .
- 10 2. An anhydrous form of sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide (Anhydrous Form C) having an X-ray powder diffraction pattern containing specific peaks at: 4.3 ($\pm 0.1^\circ$), 8.5 ($\pm 0.1^\circ$), 14.6 ($\pm 0.1^\circ$), 15.3 ($\pm 0.1^\circ$), 16.1 ($\pm 0.1^\circ$), 17.4 ($\pm 0.1^\circ$), 18.7 ($\pm 0.1^\circ$), 20.5 ($\pm 0.1^\circ$), 22.1 ($\pm 0.1^\circ$), 22.6 ($\pm 0.1^\circ$), 23.1 ($\pm 0.1^\circ$) and 29.6 ($\pm 0.1^\circ$) 2θ .
- 15 3. A hydrated form of sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide (Hydrate Form A) having an X-ray powder diffraction pattern containing specific peaks at: 4.2 ($\pm 0.1^\circ$), 8.2 ($\pm 0.1^\circ$), 8.5 ($\pm 0.1^\circ$), 9.1 ($\pm 0.1^\circ$), 11.5 ($\pm 0.1^\circ$), 12.7 ($\pm 0.1^\circ$), 14.8 ($\pm 0.1^\circ$), 15.4 ($\pm 0.1^\circ$), 16.6 ($\pm 0.1^\circ$), 17.4 ($\pm 0.1^\circ$), 17.7 ($\pm 0.1^\circ$), 18.2 ($\pm 0.1^\circ$), 20.4 ($\pm 0.1^\circ$), 23.2 ($\pm 0.1^\circ$), 29.1 ($\pm 0.1^\circ$) and 29.8 ($\pm 0.1^\circ$) 2θ .
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4. A compound as claimed in claim 3 wherein the water of crystallisation is 3-10% w/w.
- 25 5. A hydrated form of sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide (Hydrate Form B) having an X-ray powder diffraction pattern containing specific peaks at: 4.5 ($\pm 0.1^\circ$), 7.3 ($\pm 0.1^\circ$), 8.3 ($\pm 0.1^\circ$), 13.3 ($\pm 0.1^\circ$), 14.5 ($\pm 0.1^\circ$), 14.8 ($\pm 0.1^\circ$), 15.4 ($\pm 0.1^\circ$), 16.6 ($\pm 0.1^\circ$), 18.7 ($\pm 0.1^\circ$), 20.2 ($\pm 0.1^\circ$), 21.1 ($\pm 0.1^\circ$), 21.5 ($\pm 0.1^\circ$), 21.9 ($\pm 0.1^\circ$), 22.3 ($\pm 0.1^\circ$), 23.5 ($\pm 0.1^\circ$) and 24.9 ($\pm 0.1^\circ$) 2θ .
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6. A compound as claimed in claim 5 wherein the water of crystallisation is 5-7% w/w.

7. A hydrated form of the sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide (Hydrate Form C) having an X-ray powder diffraction pattern containing specific peaks at: 4.2 ($\pm 0.1^\circ$), 7.5 ($\pm 0.1^\circ$), 8.0 ($\pm 0.1^\circ$), 11.4 ($\pm 0.1^\circ$), 12.5 ($\pm 0.1^\circ$), 15.1 ($\pm 0.1^\circ$), 15.8 ($\pm 0.1^\circ$), 17.7 ($\pm 0.1^\circ$), 18.9 ($\pm 0.1^\circ$), 20.5 ($\pm 0.1^\circ$), 21.1 ($\pm 0.1^\circ$), 22.7 ($\pm 0.1^\circ$), 24.6 ($\pm 0.1^\circ$), 26.1 ($\pm 0.1^\circ$), 27.8 ($\pm 0.1^\circ$) and 29.2 ($\pm 0.1^\circ$) 2θ .
8. A compound as claimed in claim 7 wherein the water of crystallisation is 3-10% w/w.
9. A hydrated form of the sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide (Hydrate Form D) having an X-ray powder diffraction pattern containing specific peaks at: 8.8 ($\pm 0.1^\circ$), 10.5 ($\pm 0.1^\circ$), 11.8 ($\pm 0.1^\circ$), 12.9 ($\pm 0.1^\circ$), 15.6 ($\pm 0.1^\circ$), 17.1 ($\pm 0.1^\circ$), 18.9 ($\pm 0.1^\circ$), 20.8 ($\pm 0.1^\circ$), 23.3 ($\pm 0.1^\circ$), 25.6 ($\pm 0.1^\circ$), 26.1 ($\pm 0.1^\circ$), 26.9 ($\pm 0.1^\circ$), 28.1 ($\pm 0.1^\circ$), 30.6 ($\pm 0.1^\circ$), 32.5 ($\pm 0.1^\circ$) and 33.1 ($\pm 0.1^\circ$) 2θ .
10. A solvated form of the sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide (Solvated Form E) having an X-ray powder diffraction pattern containing specific peaks at: 3.6 ($\pm 0.1^\circ$), 7.1 ($\pm 0.1^\circ$), 8.3 ($\pm 0.1^\circ$), 9.3 ($\pm 0.1^\circ$), 9.8 ($\pm 0.1^\circ$), 14.1 ($\pm 0.1^\circ$), 15.9 ($\pm 0.1^\circ$), 17.7 ($\pm 0.1^\circ$), 18.6 ($\pm 0.1^\circ$), 19.3 ($\pm 0.1^\circ$), 21.7 ($\pm 0.1^\circ$), 23.1 ($\pm 0.1^\circ$), 24.1 ($\pm 0.1^\circ$), 25.0 ($\pm 0.1^\circ$), 25.8 ($\pm 0.1^\circ$) and 26.3 ($\pm 0.1^\circ$) 2θ .
11. A crystalline form of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide (Form A) having an X-ray powder diffraction pattern containing specific peaks at: 7.3 ($\pm 0.1^\circ$), 8.5 ($\pm 0.1^\circ$), 10.6 ($\pm 0.1^\circ$), 13.4 ($\pm 0.1^\circ$), 14.7 ($\pm 0.1^\circ$), 15.4 ($\pm 0.1^\circ$), 15.9 ($\pm 0.1^\circ$), 19.9 ($\pm 0.1^\circ$), 20.2 ($\pm 0.1^\circ$), 21.7 ($\pm 0.1^\circ$), 25.8 ($\pm 0.1^\circ$) and 26.6 ($\pm 0.1^\circ$) 2θ .
12. A crystalline form of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide (Form B) having an X-ray powder diffraction pattern

containing specific peaks at: 9.9 ($\pm 0.1^\circ$), 10.5 ($\pm 0.1^\circ$), 11.0 ($\pm 0.1^\circ$), 11.6 ($\pm 0.1^\circ$), 13.3 ($\pm 0.1^\circ$), 13.9 ($\pm 0.1^\circ$), 14.9 ($\pm 0.1^\circ$), 18.0 ($\pm 0.1^\circ$), 19.0 ($\pm 0.1^\circ$), 20.4 ($\pm 0.1^\circ$), 22.2 ($\pm 0.1^\circ$) and 23.0 ($\pm 0.1^\circ$) 2 θ .

- 5 13. A pharmaceutical composition comprising a compound as claimed in claims 1 to 12 and a pharmaceutically acceptable adjuvant, diluent or carrier.
14. A compound as claimed in claims 1 to 12 for use in therapy.
- 10 15. The use of a compound as claimed in claims 1 to 12 in the manufacture of a medicament for use in therapy.
16. A method of treating a chemokine mediated disease state in a mammal suffering from, or at risk of, said disease, which comprises administering to a mammal in
15 need of such treatment a therapeutically effective amount of a compound as claimed in claims 1 to 12.
17. A process for preparing Anhydrous Form B comprising:
- 20 a. drying a water-wet or hydrated form of a sample of the sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methylbenzenesulfonamide in the presence of phosphorus pentoxide under reduced pressure; or,
- b. heating a sample of Hydrate Form A from ambient temperature to 100°C.
- 25 18. A process for preparing Anhydrous Form C comprising heating a sample of Hydrate Form B from ambient temperature to 100°C.
19. A process for preparing Hydrate Form A comprising reacting 4-(3,4-dichlorophenoxy)-1,4'-bipiperidine with 4-methylbenzenesulfonyl isocyanate in a
30 suitable solvent at ambient temperature to form *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide in the suitable solvent; adding to that concentrated aqueous sodium hydroxide solution followed by water; and:

- a. stirring the resulting mixture to allow the sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide, possibly contaminated with suitable solvent, to precipitate out with Hydrate Form A remaining after filtration and drying, or,
- b. distilling the suitable solvent and allowing Hydrate Form A to precipitate from the aqueous.

20. A process for preparing Hydrate Form A comprising adding concentrated aqueous sodium hydroxide solution to a mixture of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide in water at a temperature in the range 30-60°C and allowing the mixture to cool with the sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide precipitating and Hydrate Form A remaining after filtering and drying.

21. A process for preparing Hydrate Form A as claimed in claim 20 comprising:

- a. mixing *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide with water and heating the mixture to a temperature in the range 30-60°C; and,
- b. adding concentrated aqueous sodium hydroxide solution and allowing the mixture to cool with the sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide precipitating and Hydrate Form A remaining after filtering and drying.

22. A process for preparing Hydrate Form A comprising adding concentrated aqueous sodium hydroxide solution to *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide in a suitable organic solvent; heating the mixture and separating the aqueous layer; adding IMS and, optionally, toluene to the aqueous phase and cooling the resulting mixture; and, filtering off and drying the solid that forms.

23. A process for preparing Hydrate Form A comprising heating a mixture of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide (Form B) and aqueous sodium hydroxide; cooling the mixture and extracting the cooled mixture with dichloromethane; combining the extracts;
5 optionally reducing the volume of the combined organic extracts; cooling the dichloromethane mixture so that the sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide precipitates; and, filtering off and drying the solid that forms.
- 10 24. A process for preparing Hydrate Form A comprising drying a sample of Hydrate Form D under reduced pressure at a temperature in the range 10-100°C.
25. A process for preparing Hydrate Form A comprising drying a sample of Solvated Form E at atmospheric pressure at a temperature in the range 0-30°C.
- 15 26. A process for preparing Hydrate Form B comprising mixing a solution of 4-(3,4-dichlorophenoxy)-1,4'-bipiperidine in tetrahydrofuran with a solution of 4-methylbenzenesulfonyl isocyanate in tetrahydrofuran at a temperature in the range 15-35°C; adding aqueous sodium hydroxide solution and collecting the solid that
20 precipitates.
27. A process for preparing Hydrate Form C comprising cooling a solution of the sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide in a mixture of water and acetone from reflux to
25 around 0°C and collecting the solid product that forms.
28. A process for preparing Hydrate Form C comprising drying a sample of Solvated Form E reduced pressure at a temperature in the range 10-100°C.
- 30 29. A process for preparing Hydrate Form D comprising cooling a solution of the sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide in a mixture of water and 2-propanol from 50-80°C to 0-10°C and filtering off the residue.

30. A process for preparing Solvated Form E comprising cooling a solution of the sodium salt of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide in a mixture of water, IMS and toluene from 50-80°C to 0-10°C and filtering off the residue.
31. A process for preparing *N*-[[4-(3,4-Dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide (Form A) comprising:
- purifying *N*-[[4-(3,4-dichlorophenoxy)-[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide using reverse phase chromatography eluting with a mixture of aqueous ammonia and acetonitrile; and,
 - freeze drying the fractions containing *N*-[[4-(3,4-dichlorophenoxy)-[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide and triturating the residue with acetonitrile and then drying the residue under reduced pressure at ambient temperature.
32. A process for preparing *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide (Form A) comprising:
- heating a mixture of *N*-[[4-(3,4-dichlorophenoxy)[1,4'-bipiperidin]-1'-yl]carbonyl]-4-methyl-benzenesulfonamide Form B and acetonitrile to 40-60°C; and,
 - drying the solid from the slurry so formed under reduced pressure.